Discrete dynamic modeling of signal transduction networks

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M ODELING the dynamics of complex biological systems is challenging even when well-established biochemical frameworks are applicable. In the case of regulatory and signaling systems that include heterogeneous components and interactions, and/or are sparsely documented in terms of quantitative information, modeling is often thought impossible.

This talk will argue for the usefulness of a discrete dynamic framework in incorporating qualitative interaction information into a predictive model. I will present examples of predictive discrete dynamic models of plant drought signaling and survival signaling in cytotoxic T cells. All models are based on a reconstruction of the network of interactions among several dozen components and on qualitative interaction and activity information. The models make predictions regarding the key nodes whose (in)activity is necessary for reaching a desired outcome, such as stomatal opening or apoptosis of T cells. Several of these predictions were validated experimentally. The success of the models indicate that network-based discrete dynamic modeling is a promising framework that allows system-level analysis and predictions that would not be feasible using traditional methods.